	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
1	BRS	L1	111	hamuro adj junji.in.	USPAT; US-PGPUB; EPO; JPO;	2003/07/11 17:30			0
2	BRS	L3	19659	glutathione or GSH	USPAT; US-PGPUB; EPO; JPO;	2003/07/11 17:34			0
3	BRS	L5	28596	macrophage	USPAT; US-PGPUB; EPO; JPO;	2003/07/11 17:35			0
4	BRS	L6	242	3 same 5	USPAT; US-PGPUB; EPO; JPO;	2003/07/11 17:35			0
5	BRS	L7	7	1 and 6	USPAT; US-PGPUB; EPO; JPO;	2003/07/11 17:36			0
6	BRS	L8	1548	(reductive adj glutathione) or GSH	USPAT; US-PGPUB; EPO; JPO;	2003/07/11 17:42			0
7	BRS	L9	35	5 same 8	USPAT; US-PGPUB; EPO; JPO;	2003/07/11 17:42			0
8	BRS	L10	8192	il-6	USPAT; US-PGPUB; EPO; JPO;	2003/07/11 17:43			0
9	BRS	L11	851	il-12 same NO	USPAT; US-PGPUB; EPO; JPO;	2003/07/11 17:44			0
10	BRS	L13	430	10 same 11	USPAT; US-PGPUB; EPO; JPO;	2003/07/11 17:45			0

	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
11	BRS	L14	2	6 same 13	USPAT; US-PGPUB; EPO; JPO;	2003/07/11 17:47			0
12	BRS	L15	37304	immune adj response	USPAT; US-PGPUB; EPO; JPO;	2003/07/11 17:48			0
13	BRS	L16	5141	th2	USPAT; US-PGPUB; EPO; JPO;	2003/07/11 17:48			0
14	BRS	L17	968	15 same 16	USPAT; US-PGPUB; EPO; JPO;	2003/07/11 17:48			0
15	BRS	L18	2	6 same 17	USPAT; US-PGPUB; EPO; JPO;	2003/07/11 17:48			0
16	BRS	L19	33980	(gastrointestinal adj inflammatory adj disease) or (chronic adj rheumatoid adj arthritis) or hepatitis or (hepatic adj cirrhosis)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/11 17:50			0
17	BRS	L20	6	19 same 6	USPAT; US-PGPUB; EPO; JPO;	2003/07/11 17:50			0

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FILE 'MEDLINE' ENTERED AT 17:57:17 11 JUL 2003

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FILE 'AGRICOLA' ENTERED AT 17:57:17 ON 11 JUL 2003

=> s (reductive glutathione) or GSH
L1       70188 (REDUCTIVE GLUTATHIONE) OR GSH

=> s macrophage
L2      604771 MACROPHAGE

=> s l1 (p) l2
L3        1122 L1 (P) L2

=> s th2
L4       50239 TH2

=> s l3 (p) l4
L5          26 L3 (P) L4

=> s il-6 (p) il-12 (p) NO
L6        1312 IL-6 (P) IL-12 (P) NO

=> s l5 (p) l6
L7           4 L5 (P) L6

=> duplicate remove l7
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L7
L8            1 DUPLICATE REMOVE L7 (3 DUPLICATES REMOVED)

=> d l8 1 ibib abs

L8   ANSWER 1 OF 1     MEDLINE                              DUPLICATE 1
ACCESSION NUMBER:   2002269797     MEDLINE
DOCUMENT NUMBER:    22004751   PubMed ID: 12013506
TITLE:              The skewing to Th1 induced by lentinan is directed through
                    the distinctive cytokine production by macrophages with
                    elevated intracellular glutathione content.
AUTHOR:             Murata Yukie; Shimamura Toshiro; Tagami Tomoyuki; Takatsuki
                    Fumihiko; Hamuro Junji
CORPORATE SOURCE:   Basic Research Institute, Ajinomoto Central Research
                    Laboratories, Ajinomoto Co. Inc., Kawasaki, Japan.
SOURCE:             Int Immunopharmacol, (2002 Apr) 2 (5) 673-89.
                    Journal code: 100965259. ISSN: 1567-5769.
PUB. COUNTRY:       Netherlands
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200211
ENTRY DATE:         Entered STN: 20020516
                    Last Updated on STN: 20021211
                    Entered Medline: 20021122
AB   In vivo lentinan (LNT)-elicited peritoneal   ***macrophages***   (Mps)
     showed the reduced release of prostaglandins (PGs), IL-10 and   ***IL***
     -  ***6***  , while it endowed Mps with the elevated capability to produce
       ***IL***  -  ***12***   and nitric oxide (  ***NO***  ) upon in vitro
     triggering, due to the elevated intracellular glutathione (  ***GSH***  )
     content in Mps.  Deprivation of intracellular   ***GSH***   completely
     ablated the production of   ***IL***  -  ***12***  .  Conversely,
     lipopolysaccharide (LPS) induced peritoneal Mps with the reduced
     intracellular   ***GSH***   content and the reciprocal profile of mediator
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production. Mps with the elevated intracelluar ***GSH*** [redacted]
arbitrarily termed as reducti[redacted]Mp (RMp) and that with reduced[redacted]ount as
oxidative Mp (OMp). OMp was converted to RMp when ***GSH*** was
replenished with glutathione monoethylester (***GSH*** -OEt). The IL-2
administration in combination with LNT exerted the synergistic induction
of RMp, resulting in synergistic augmentation of ***IL*** - ***12***
, ***NO*** and reduction of ***IL*** - ***6*** production. It
was also confirmed that CD4+T cells derived of LNT-administered mice
showed augmented IFN-gamma and reduced IL-4 production upon in vitro
anti-CD3 stimulation. Taken together it is concluded that skewing of Th1/
Th2 balance to Th1 by a beta-(1-3)-glucan, LNT, is directed
through the distinctive production of ***IL*** - ***12*** versus
IL - ***6*** , IL-10 and prostaglandin E2 (PGE2) by Mps,
depending on intracellular ***GSH*** redox status. To the efficient
tumor immunotherapy, it may be one of the critical elements to induce a
reductive form of Mps in tumor stromal tissues to maintain Th1 response.

=> d his

(FILE 'HOME' ENTERED AT 17:56:57 ON 11 JUL 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
17:57:17 ON 11 JUL 2003
L1 70188 S (REDUCTIVE GLUTATHIONE) OR GSH
L2 604771 S MACROPHAGE
L3 1122 S L1 (P) L2
L4 50239 S TH2
L5 26 S L3 (P) L4
L6 1312 S IL-6 (P) IL-12 (P) NO
L7 4 S L5 (P) L6
L8 1 DUPLICATE REMOVE L7 (3 DUPLICATES REMOVED)

=> duplicate remove l5
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n
PROCESSING COMPLETED FOR L5
L9 9 DUPLICATE REMOVE L5 (17 DUPLICATES REMOVED)

=> s l9 not l8
L10 8 L9 NOT L8

=> d l10 1-8 ibib abs

L10 ANSWER 1 OF 8 MEDLINE
ACCESSION NUMBER: 2002147939 MEDLINE
DOCUMENT NUMBER: 21831033 PubMed ID: 11841834
TITLE: Intracellular thiol redox status of macrophages directs the Th1 skewing in thioredoxin transgenic mice during aging.
AUTHOR: Murata Yukie; Amao Michiko; Yoneda Junya; Hamuro Junji
CORPORATE SOURCE: Basic Research Institute, Ajinomoto Central Research Laboratories, Ajinomoto Co. Inc., 1-1 Suzuki-cho, Kawasaki-ku, 210-0861, Kawasaki, Japan.
SOURCE: MOLECULAR IMMUNOLOGY, (2002 Feb) 38 (10) 747-57. Journal code: 7905289. ISSN: 0161-5890.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200204
ENTRY DATE: Entered STN: 20020308
Last Updated on STN: 20020410
Entered Medline: 20020409
AB We have been proposing the functional distinction of two classes of ***macrophages*** (Mp), namely the reductive ***macrophages*** (RMp) with high intracellular content of glutathione (***GSH***) and the oxidative ***macrophages*** (OMp) with reduced content. At the same time we have been investigating the variation of RMp/OMp balance during aging of mice, especially in relation to the age related onset of autoimmune diseases. In this paper we have investigated the Th1/ ***Th2*** balance of thioredoxin (TRX) transgenic (Tg) mice, with prolonged life longevity, during aging in the context of the intracellular redox status of Mp, which has been hypothesized to be crucial in regulating the Th1/ ***Th2*** balance. It was confirmed that peritoneal resident Mp of Tg mice showed the higher ***GSH*** /GSSG ratios compared with that of age matched wild type (WT) mice. The predominance of RMp was associated with the sustained maintenance of Th1

prevalence during aging until [redacted] years in Tg mice, whereas WT littermates showed rapid polarization to [redacted]***Th2***[redacted] around the age of [redacted] months. The Tg mice showed elevation of IFN-gamma and reduction of IL-10 with moderate change of IL-4 produced by CD4+ T cells. The WT mice showed inverse changes of IFN-gamma/IL-4 and IFN-gamma/IL-10 ratios during aging. In addition, IL-10 production by Mp was dramatically reduced in aged Tg mice. Thus, TRX Tg mice may be useful to investigate the contribution of the anti-oxidant defense mechanism during aging accompanied with increasing oxidative stress.

L10 ANSWER 2 OF 8 MEDLINE
ACCESSION NUMBER: 2001364628 MEDLINE
DOCUMENT NUMBER: 21315494 PubMed ID: 11422207
TITLE: Regulation of LPS induced IL-12 production by IFN-gamma and IL-4 through intracellular glutathione status in human alveolar macrophages.
AUTHOR: Dobashi K; Aihara M; Araki T; Shimizu Y; Utsugi M; Iizuka K; Murata Y; Hamuro J; Nakazawa T; Mori M
CORPORATE SOURCE: First Department of Internal Medicine, Gunma University Faculty of Medicine, School of Medicine, Maebashi, Gunma, Japan.. dobashik@med.gunma-u.ac.jp
SOURCE: CLINICAL AND EXPERIMENTAL IMMUNOLOGY, (2001 May) 124 (2) 290-6.
Journal code: 0057202. ISSN: 0009-9104.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200107
ENTRY DATE: Entered STN: 20010716
Last Updated on STN: 20010716
Entered Medline: 20010712
AB Interleukin-12 (IL-12) is secreted from monocytes and ***macrophages*** ; it exerts pleiotropic effects on T cells and natural killer (NK) cells, and stimulates interferon-gamma (IFN-gamma) secretion. Glutathione tripeptide regulates the intracellular redox status and other aspects of cell physiology. We examined whether IFN-gamma and IL-4 affect the balance between intracellular reduced glutathione (***GSH***) and oxidized (GSSG) glutathione, as this may affect IL-12 production in human alveolar ***macrophages*** (AM). We used both AM from healthy non-smokers obtained by bronchoalveolar lavage and the monocytic THP-1 cell line in this study. Incubation of AM for 2 h with the ***GSH*** precursor N-acetylcysteine (NAC) increased the intracellular ***GSH*** /GSSG ratio, and enhanced lipopolysaccharide (LPS)-induced IL-12 secretion by AM. In THP-1 cells, NAC increased the ***GSH*** /GSSG ratio and the expression of LPS-induced IL-12 mRNA, whereas L-buthionine-[S,R]-sulphoximine (BSO) decreased these. NAC and BSO offset their own effects on the intracellular ***GSH*** /GSSG ratio and the expression of LPS-induced IL-12 mRNA. Furthermore, exposure of AM to the helper T cell type 1 (Th1) cytokine IFN-gamma or the helper T cell type 2 (***Th2***) cytokine IL-4 for 72 h increased and decreased the ***GSH*** /GSSG ratio, respectively. Lipopolysaccharide (LPS)-induced secretion of IL-12 in AM was enhanced by IFN-gamma but inhibited by IL-4. These results suggest that IFN-gamma and IL-4 oppositely affect the ***GSH*** /GSSG balance, which may regulate IL-12 secretion from AM in response to LPS.

L10 ANSWER 3 OF 8 MEDLINE
ACCESSION NUMBER: 2001272993 MEDLINE
DOCUMENT NUMBER: 21260833 PubMed ID: 11367535
TITLE: Suppression of allergic reactions by royal jelly in association with the restoration of macrophage function and the improvement of Th1/Th2 cell responses.
AUTHOR: Oka H; Emori Y; Kobayashi N; Hayashi Y; Nomoto K
CORPORATE SOURCE: Central Research Laboratories, Zeria Pharmaceutical Co., Ltd., 2512-1 Oshikiri, Kohnan-machi, Ohsato-gun, Saitama 360-0111, Japan.
SOURCE: Int Immunopharmacol, (2001 Mar) 1 (3) 521-32.
Journal code: 100965259. ISSN: 1567-5769.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200106
ENTRY DATE: Entered STN: 20010702
Last Updated on STN: 20010702
Entered Medline: 20010628
AB We studied the immunomodulatory effects of royal jelly (RJ), the principal

food source of the queen honeybee. In this study, suppression of allergic reactions by RJ was investigated in DNP-KLH immunized mice (DNP-KLH mice). Oral administration of RJ (1 g/kg) to DNP-KLH mice significantly decreased the serum levels of antigen-specific Ig E and significantly inhibited DNP-KLH mediated-histamine release from mast cells, resulting in the suppression of immediate hypersensitivity reactions of ear skin. In DNP-KLH mice, IFN-gamma (Th1 cytokine) production from CD4+ T cells was suppressed and IL-4 (***Th2*** cytokine) production from CD4+ T cells was increased as compared to normal mice. On the other hand, RJ improved the balance of Th1/ ***Th2*** cell responses from ***Th2*** -dominant to Th1-dominant. RJ significantly increased ***GSH*** levels in ***macrophages*** from DNP-KLH mice. In addition, the administration of RJ to DNP-KLH mice increased IL-12 p40 mRNA expression and NO production, and decreased PG E2 production from ***macrophages*** as compared to untreated DNP-KLH mice. These results suggested that RJ suppressed antigen-specific Ig E production and histamine release from mast cells in association with the restoration of ***macrophage*** function and improvement of Th1/ ***Th2*** cell responses in DNP-KLH mice.

L10 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:478908 CAPLUS
DOCUMENT NUMBER: 137:91884
TITLE: The conversion of redox status of peritoneal macrophages during pathological progression of spontaneous inflammatory bowel disease in Janus family tyrosine kinase 3-/- and IL-2 receptor .gamma.-/- mice
AUTHOR(S): Murata, Yukie; Yamashita, Akira; Saito, Takashi; Sugamura, Kazuo; Hamuro, Junji
CORPORATE SOURCE: Basic Research Laboratories, Ajinomoto Co. Inc., Kawasaki, 210-0861, Japan
SOURCE: International Immunology (2002), 14(6), 627-636
CODEN: INIMEN; ISSN: 0953-8178
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The distinct thiol redox status in ***macrophages*** , either elevated or reduced intracellular content of glutathione (***GSH***), was confirmed during aging in IL-2 receptor (IL-2R).gamma. and Janus family tyrosine kinase (JAK)3 gene-disrupted mice. Oxidative ***macrophages*** (OMp) with reduced ***GSH*** dominated initially at a younger age in both mice. OMp-dominated JAK3 or IL-2R.gamma. chain-deficient mice showed shortened life longevity compared with wild-type littermates. These mice elicited spontaneous onsets of inflammatory bowel disease (IBD)-like symptoms accompanied with the conversion of the redox status of ***macrophages*** to reductive phenotypes with elevated intracellular ***GSH*** . Conversion of OMp to the reductive phenotype by ***GSH*** monoethyl ester or by a .beta.-(1-3)-glucan accelerated the disease onset, concomitant with the skewing from ***Th2*** to Th1 responses. On the contrary, N,N-diacetyl cystine dimethylester, which is capable of inducing OMp, delayed the incidence of IBD-like symptoms and improved the survival rate. This implies that the conversion of OMp/ ***Th2*** to reductive ***macrophages*** /Th1 may be crit. for the disease progression. The study of these mice may provide insight into the mechanisms underlying Crohn's disease and ulcerative colitis.
REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:712139 CAPLUS
DOCUMENT NUMBER: 132:221210
TITLE: The triggering and healing of tumor stromal inflammatory reactions regulated by oxidative and reductive macrophages
AUTHOR(S): Hamuro, Junji; Murata, Yukie; Suzuki, Manabu; Takatsuki, Fumihiko; Suga, Tetsuya
CORPORATE SOURCE: Basic Research Laboratories, Ajinomoto Co., Inc., Kanagawa, 210-0801, Japan
SOURCE: Gann Monograph on Cancer Research (1999), 48(Recent Advances of Human Tumor Immunology and Immunotherapy), 153-164
CODEN: GMCRDC; ISSN: 0072-0151
PUBLISHER: Japan Scientific Societies Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Pre- and post-operative administration of lentinan (LNT) in combination with interleukin-2 (IL-2) showed complete cure in murine tumor models due

to synergistic augmentation of the tumor tissue stromal reaction including lymphoreticular infiltrates and the formation of reticular fib[redacted]. The cellular reactions at tumor tissues are frequently accompanied by the conversion of the reaction into an oxidative inflammatory reaction by locally produced cytokines. LNT induced ***macrophages*** (M.vphi.s) showed reduced release of prostaglandins and IL-6, while they showed elevated prodn. of IL-12, due to the increase of cellular glutathione (***GSH***). Conversely, lipopolysaccharide (LPS) induced ***macrophages*** with reduced ***GSH*** content. M.vphi.s with a high content of ***GSH*** are called reductive M.vphi.s and those with a reduced amt. oxidative M.vphi.s. Helper T cell type 1, 2 (TH1/ ***TH2***) balance is largely regulated by the balance between reductive and oxidative M.vphi.s through the balance of the prodn. of IL-12 vs. IL-6 from M.vphi.s. To keep tumor specific immune response working efficiently, it may be important to maintain the TH1 responses and the predominance of a reductive form of M.vphi. in tumor tissue stromal inflammation, in the context of tissue remodelling after extravasation and infiltration of immune cells into tumor tissues.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:277457 CAPLUS
DOCUMENT NUMBER: 130:322683
TITLE: Classification of macrophages, disease diagnosis, system and kit for the diagnosis, and screening or monitoring of pharmaceuticals for immunological disease treatment
INVENTOR(S): Hamuro, Junji; Murata, Yukie
PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 13 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 11118792	A2	19990430	JP 1997-303426	19971017

PRIORITY APPLN. INFO.: JP 1997-303426 19971017

AB Macrophages are classified into oxidized and reduced types having different functions, by (in)directly detg. oxidized glutathione (GSSG) and/or reduced glutathione (GSH) in the macrophages. Immunol. diseases and/or cancer are diagnosed by detg. oxidized- and/or reduced-type macrophages using reagents such as monochlorobimane. Oxidized- and/or reduced-type macrophages in body fluids or cells are detd. for screening or monitoring of pharmaceuticals, for treatment or prevention of immunol. diseases.

L10 ANSWER 7 OF 8 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000125168 EMBASE
TITLE: Inhibitory effect of royal jelly on allergic reactions through the regulation of Th1/Th2 cell responses.
AUTHOR: Oka H.; Emori Y.; Kobayashi N.; Hayashi Y.; Nomoto K.
CORPORATE SOURCE: Dr. Y. Hayashi, Central Research Laboratories, Zeria Pharmaceutical Co., Ltd., 2512-1 Oshikiri, Kohnan-machi, Ohsato-gun, Saitama 360-0111, Japan
SOURCE: Biotherapy, (2000) 14/2 (145-150).
Refs: 20
ISSN: 0914-2223 CODEN: BITPE
COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
037 Drug Literature Index
LANGUAGE: Japanese
SUMMARY LANGUAGE: English; Japanese

AB We have studied the immunomodulatory effects of royal jelly (RJ), a principal food of the queen honey bee. In this paper, suppression of allergic reactions by RJ was investigated in mice immunized with DNP-KLH (DNP-KLH mice). Oral administration of RJ (1 g/kg) to DNP-KLH mice significantly decreased the serum level of IgE, and significantly inhibited DNP-KLH mediated-histamine release from mast cells. In DNP-KLH mice, IFN-.gamma. (Th1 cytokine) production was suppressed and IL-4 (***Th2*** cytokine) production was increased as compared to normal mice. On the other hand, RJ restored the balance of Th1/ ***Th2*** cell responses from a ***Th2*** dominant state to a normal state. RJ

significantly increased glutathione (***GSH***) levels in ***macrophages*** from DNP-KLH mice. These results suggest that RJ restored ***GSH*** levels and Th cell responses, resulting in the suppression of IgE production and the inhibition of mast cell degranulation in DNP-KLH mice.

L10 ANSWER 8 OF 8 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 96170609 EMBASE
DOCUMENT NUMBER: 1996170609
TITLE: Lentinan regulates the local inflammatory cellular reaction at tumor tissues - Its relation with antitumor effects.
AUTHOR: Hamuro J.
CORPORATE SOURCE: Ajinomoto Co., Inc., Basic Research Institute, 1-1 Suzuki-cho,Kawasaki-ku, Kawasaki 210, Japan
SOURCE: Biotherapy, (1996) 10/4 (581-588).
ISSN: 0914-2223 CODEN: BITPE
COUNTRY: Japan
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
026 Immunology, Serology and Transplantation
LANGUAGE: Japanese
SUMMARY LANGUAGE: English; Japanese
AB Either immunotherapy or chemotherapy requires anticachectic treatments to improve its therapeutic effects leading to life prolongation. Cachexia is mainly induced by oxidative local cellular inflammatory reactions at tumor tissues by production of PGE2, reactive oxygen intermediates and cachectic/immunosuppressive cytokines such as IL-6, IL-1, TNF and TGF-.beta.. To induce the efficient specific immunological responses to tumor antigens, it is necessary to induce cellular reactions at tumor tissues to break the dormant state (ignorance of tumor antigens by host immune systems). The induction of cellular reactions at tumor tissues is confronted frequently with the conversion of cellular reactions into oxidative inflammatory reactions via overactivation of ***macrophages*** (M.phi.) and neutrophils. Lentinan suppresses the conversion and maintain the redox state of M.phi. at the reduced state designated by the high content of the reduced form of glutathione (***GSH***). M.phi.s with the high content of ***GSH*** respond to TH1 cytokines to produce an increased amount of NO and a reduced amount of IL-6, whereas M.phi.s with decreased ***GSH*** content respond in a manner resulting in inverse effects. In the advanced stage of cancer patients, the oxidative M.phi.s are responsible for the induction of ***TH2*** cytokines responses resulting in the induction of cachexia.

=> d his

(FILE 'HOME' ENTERED AT 17:56:57 ON 11 JUL 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 17:57:17 ON 11 JUL 2003
L1 70188 S (REDUCTIVE GLUTATHIONE) OR GSH
L2 604771 S MACROPHAGE
L3 1122 S L1 (P) L2
L4 50239 S TH2
L5 26 S L3 (P) L4
L6 1312 S IL-6 (P) IL-12 (P) NO
L7 4 S L5 (P) L6
L8 1 DUPLICATE REMOVE L7 (3 DUPLICATES REMOVED)
L9 9 DUPLICATE REMOVE L5 (17 DUPLICATES REMOVED)
L10 8 S L9 NOT L8

=> s immune response
L11 371111 IMMUNE RESPONSE

=> s l4 (p) l11
L12 11463 L4 (P) L11

=> s l3 (p) l12
L13 2 L3 (P) L12

=> duplicate remove l13
DUPLICATE PREFERENCE IS 'CAPLUS, EMBASE'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n
PROCESSING COMPLETED FOR L13
L14 1 DUPLICATE REMOVE L13 (1 DUPLICATE REMOVED)

=> d l14 1 ibib abs

L14 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 1

ACCESSION NUMBER: 1999:712139 CAPLUS
DOCUMENT NUMBER: 132:221210
TITLE: The triggering and healing of tumor stromal inflammatory reactions regulated by oxidative and reductive macrophages
AUTHOR(S): Hamuro, Junji; Murata, Yukie; Suzuki, Manabu; Takatsuki, Fumihiko; Suga, Tetsuya
CORPORATE SOURCE: Basic Research Laboratories, Ajinomoto Co., Inc., Kanagawa, 210-0801, Japan
SOURCE: Gann Monograph on Cancer Research (1999), 48(Recent Advances of Human Tumor Immunology and Immunotherapy), 153-164
CODEN: GMCRDC; ISSN: 0072-0151
PUBLISHER: Japan Scientific Societies Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Pre- and post-operative administration of lentinan (LNT) in combination with interleukin-2 (IL-2) showed complete cure in murine tumor models due to synergistic augmentation of the tumor tissue stromal reaction including lymphoreticular infiltrates and the formation of reticular fibers. The cellular reactions at tumor tissues are frequently accompanied by the conversion of the reaction into an oxidative inflammatory reaction by locally produced cytokines. LNT induced ***macrophages*** (M.vphi.s) showed reduced release of prostaglandins and IL-6, while they showed elevated prodn. of IL-12, due to the increase of cellular glutathione (***GSH***). Conversely, lipopolysaccharide (LPS) induced ***macrophages*** with reduced ***GSH*** content. M.vphi.s with a high content of ***GSH*** are called reductive M.vphi.s and those with a reduced amt. oxidative M.vphi.s. Helper T cell type 1, 2 (TH1/ ***TH2***) balance is largely regulated by the balance between reductive and oxidative M.vphi.s through the balance of the prodn. of IL-12 vs. IL-6 from M.vphi.s. To keep tumor specific ***immune*** ***response*** working efficiently, it may be important to maintain the TH1 responses and the predominance of a reductive form of M.vphi. in tumor tissue stromal inflammation, in the context of tissue remodelling after extravasation and infiltration of immune cells into tumor tissues.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 17:56:57 ON 11 JUL 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 17:57:17 ON 11 JUL 2003

L1 70188 S (REDUCTIVE GLUTATHIONE) OR GSH
L2 604771 S MACROPHAGE
L3 1122 S L1 (P) L2
L4 50239 S TH2
L5 26 S L3 (P) L4
L6 1312 S IL-6 (P) IL-12 (P) NO
L7 4 S L5 (P) L6
L8 1 DUPLICATE REMOVE L7 (3 DUPLICATES REMOVED)
L9 9 DUPLICATE REMOVE L5 (17 DUPLICATES REMOVED)
L10 8 S L9 NOT L8
L11 371111 S IMMUNE RESPONSE
L12 11463 S L4 (P) L11
L13 2 S L3 (P) L12
L14 1 DUPLICATE REMOVE L13 (1 DUPLICATE REMOVED)

=> s (gastrointestinal inflammatory disease) or (chronic rheumatoid arthritis) or hepatitis or (he
5 FILES SEARCHED...
L15 430583 (GASTROINTESTINAL INFLAMMATORY DISEASE) OR (CHRONIC RHEUMATOID ARTHRITIS) OR HEPATITIS OR (HEPATIC CIRRHOSIS)

=> s l15 (p) l3
L16 1 L15 (P) L3

=> s l16 not (l14 or l10 or l8)
L17 1 L16 NOT (L14 OR L10 OR L8)

=> d l17 1 ibib abs

L17 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:204853 CAPLUS
DOCUMENT NUMBER: 137:21088
TITLE: Pharmacological studies on certain mushrooms from China
AUTHOR(S): Ooi, Vincent E. C.
CORPORATE SOURCE: Department of Biology, The Chinese University of Hong Kong, Shatin, Peop. Rep. China
SOURCE: International Journal of Medicinal Mushrooms (2001), 3(4), 341-354
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AB This article focuses mainly on biopharmacol. studies of selected Chinese medicinal mushrooms, namely the immunomodulation and antitumor activity of Tricholoma giganteum Massee, blood pressure lowering action and mechanism of Volvariella volvacea (Bull.: Fr.) Sing., and the liver protective effect of Trametes versicolor (L.: Fr.) Lloyd. A polysaccharide-protein complex (PSPC) isolated from the culture filtrates of T. giganteum inhibited the growth of solid Sarcoma 180 in mice, with no sign of toxicity. PSPC showed immunomodulating action in vivo. It restored and increased phagocytic function of peritoneal exudate cells (***macrophages***) of the tumor-bearing mice. It also exhibited indirect cytotoxicity against P815 and L929 by activating ***macrophages*** to release the mediators, such as nitric oxide (NO) and tumor necrosis factor-.alpha. (TNF-.alpha.). The direct cytotoxicity of PSPC was obsd. in PU5-1.8, H3B, HL-60, and melanoma cell lines. The antiproliferative activity against PU5-1.8 cells was strong at a dose of 60 .mu.g/mL of PSPC. Therefore, the antitumor activity of PSPC might be due to both host-mediated immunomodulating action and direct cytotoxicity to cancer cells. A fraction isolated from the fruiting bodies of Volvariella volvacea (VE), with a mol. mass of about 10 kDa, was heat stable and resistant to trypsin digestion. The blood pressure changes produced by the ext. alone or in the presence of various specific agonists or antagonists were investigated. An i.v. injection of VE produced a hypotensive effect in normotensive rats with an ED50 of 25 mg dry wt./kg body wt. This hypotensive effect of VE was attenuated or blunted in the presence of hexamethonium, phentolamine, pyrilamine, and cimetidine suggesting the involvement of the .alpha.-adrenergic component of the autonomic system and/or histaminergic stimulation. The contractile response could be inhibited by the antagonists of serotonin and .alpha.-adrenoceptor, ketanserin, and phentolamine, resp. It is likely that VE contained serotonin-like substances because the mechanism of action of VE was similar to that of serotonin. The protective effects of polysaccharide peptide (PSP) of Trametes versicolor on hepatotoxicity were investigated using carbon tetrachloride (CCI4)-induced and paracetamol (APAP)-induced liver injury in the rat as the chem. ***hepatitis*** models. A toxic dose of CCI4 (1.25 mL/kg) raised the levels of serum glutamic pyruvic transaminase (SGPT) and that of glutamic oxaloacetic transaminase (SGOT) in the exptl. rats. PSP significantly reduced the elevated levels of both the SGPT and SGOT in rats exposed to CCI4. Similarly, a single oral dose of 1.0 g/kg of APAP was able to produce significantly elevated levels of SGPT and SGOT. I.p. administration of 300 mg/kg of PSP could significantly reduce the APAP-induced acute elevation in the levels of SGPT and SGOT in rats. PSP probably acts to prevent the fall of hepatic reduced glutathione (***GSH***) though some ***GSH*** -dependent enzymes and preserve the structural integrity of the cellular membrane of hepatocytes, or probably protect paracetamol-induced liver injury through their antioxidant properties acting as a scavenger of free radicals even at low levels of ***GSH*** .

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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(FILE 'HOME' ENTERED AT 17:56:57 ON 11 JUL 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 17:57:17 ON 11 JUL 2003

L1 70188 S (REDUCTIVE GLUTATHIONE) OR GSH
L2 604771 S MACROPHAGE
L3 1122 S L1 (P) L2
L4 50239 S TH2
L5 26 S L3 (P) L4
L6 1312 S IL-6 (P) IL-12 (P) NO

L7 4 S L3 (P) L6
L8 1 DUPLICATE REMOVE L[redacted]3 DUPLICATES REMOVED)
L9 9 DUPLICATE REMOVE L[redacted](17 DUPLICATES REMOVED)
L10 8 S L9 NOT L8
L11 371111 S IMMUNE RESPONSE
L12 11463 S L4 (P) L11
L13 2 S L3 (P) L12
L14 1 DUPLICATE REMOVE L13 (1 DUPLICATE REMOVED)
L15 430583 S (GASTROINTESTINAL INFLAMMATORY DISEASE) OR (CHRONIC RHEUMATOI
L16 1 S L15 (P) L3
L17 1 S L16 NOT (L14 OR L10 OR L8)

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